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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,784	06/19/2001	Sara Petersen Bjorn	0459-0615P	8714
2292	7590	02/25/2004	EXAMINER	
BIRCH STEWART KOLASCH & BIRCH PO BOX 747 FALLS CHURCH, VA 22040-0747			ROBINSON, HOPE A	
		ART UNIT	PAPER NUMBER	
		1653		

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,784	BJORN ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 03 December 2003.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-6 and 8-21 is/are pending in the application.
- 4a) Of the above claim(s) 10, 13-19 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-6,8,9,11,12,20 and 21 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: _____.

DETAILED ACTION

1. Applicant's response to the Office Action mailed June 17, 2003 on December 3, 2003 is acknowledged.

Claim Disposition

2. Claim 7 has been canceled. Claims 1-2 have been amended. Claims 1-6 and 8-21 are pending. Claims 1-6, 8-9, 11-12 and 20-21 (SEQ ID NO: 4) are under examination.
3. The following grounds of rejection are or remain applicable:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 1-6, 8-9, 11-12 and 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because the claim recites, "wherein the amino acid in position 1 preceding the chromophore has been substituted" and there is no indicia of what the substitution is to define the claimed structure. Note that the claim describes a substitution at position 222 only. In addition, the claim does not presently recite the

structure of the GFP protein that is to undergo the recited modifications, thus the claims is not complete. The dependent claims hereto are also included in this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

6. Claims 1-6 and 8 remain rejected under 35 U.S.C. 103 (a) as being unpatentable over Thastrup et al. (WO 97/11094 March 27, 1997) in view of Ehrig et al. (FEBS Letters, vol. 367, pages 163-166, 1995).

Thastrup et al. teach a fluorescent protein derived from GFP (Aequorea green fluorescent protein) or any functional analogue thereof wherein the amino acid in position 1 preceding the chromophore has been mutated to provide an increase of fluorescence intensity. Thastrup et al. teach that the proteins exhibit high fluorescence in cells expressing them when said cells are incubated at a temperature of 30 degrees or above. Thastrup et al. also teach that the chromophore is in position 65-67 and the substitution of F at position 64 for an aliphatic amino acid (see pages 1-4, claims 1-4 of the instant application). Thastrup et al. teach that the preferred mutation is F64L (claims 5-6), however, deletions, substitutions, insertions or posttranslational modifications immediately preceding the chromophore are also included in the invention, however is silent on the E222G mutation recited in claim 1 of the instant specification. However, Ehrig et al. teach the E222G mutation (see abstract, claims 1 and 8). Ehrig et al. teach a single amino acid change producing a mutant of GFP (E22G).

Therefore, it would have obvious for one of ordinary skill in the art at the time the invention was made to modify the teachings of Thastrup et al. (GFP mutation F64L) by adding in the teachings of Ehrig et al. (GFP E222G) to arrive at the claimed invention as a whole. One of ordinary skill in the art would be motivated to combine the teachings of the references because Thastrup et al., disclose that other mutations are possible preceding the chromophore provided that they result in improved fluorescence properties of the various fluorescent proteins (page 4, lines 10-15) and Ehrig teach such

a mutation. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

The response filed on December 3, 2003 has been considered. The rejections of record have been maintained. Note however, that the rejection of record under 35 U.S.C. 112, second paragraph has been clarified with respect to the structure of the protein needed in the claim. In addition, although applicant amended the claims to recite "substituted" in lieu of "mutated", the structure remains undefined as there is no indication of what residues will be substituted. Claim 1 to be definite requires the recitation of a sequence for the GFP and the specific substitutions that can be tolerated by this sequence at the position 1 preceding the chromophore.

Note that art rejection remains. Applicant's response states that the claimed invention involves a combination of the F64L and E222G mutations of GFP. However, this argument is not convincing as the combined teaching of the references renders the invention as obvious. The rejection under 35 USC 103 above is consistent with case law. Applicants are referred to *In re Kerkoven* (205 USPQ 1069) in which it was shown to be *prima facia* obvious to combine two compositions, each of which is taught by the prior art to be used for that very same purpose. *Ex Parte Quadranti* (25 USPQ2d 1071) also sets forth this precedent, in that the use of materials in combination, each of which is known to function for the intended purpose, is generally held to be *prima facia* obvious. *Ex parte Kucera* (165 USPQ 332) clearly states that synergism has no magical status in rendering otherwise obvious subject matter patentable. Therefore, then,

barring unexpected results, one would reasonably expect enhanced, additive, or synergistic activity to be observed by combining the compositions or materials.

Applicant also states that the claimed invention results in an excitation of 470 nm compared to 481nm disclosed in Ehrig et al. This argument is not convincing because the claims do not recite the stated excitation maximum as a limitation to the claims. As stated above Ehrig et al. rectifies the silent teaching of Thastrup et al. with regard to the point mutation found at E222 and teaches the substitution of E to G, thus rendering obvious the claimed invention.

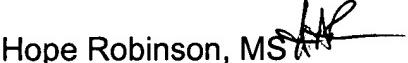
Conclusion

7. No claims are presently allowable.

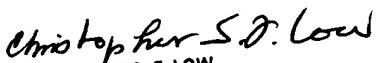
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Hope Robinson, M.S.

Patent Examiner


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